LISTING OF CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application:

Claims 1-21. (Canceled as prosecuted in a previous application)

Claim 22. (Currently Amended): A method of inserting a heterologous gene coding sequence into an endogenous gene in a mouse embryonic stem cell genome and expressing said heterologous gene coding sequence, comprising the step of transforming the mouse embryonic stem cell with a random gene trap vector comprising a DNA construct, wherein the heterologous gene coding sequence lacks a promoter, and (ii) comprises the sequence:

5' X-A-P-B-Q-C-Y 3'

in which

X and Y are separately, DNA sequences substantially homologous with a host gene locus;

P is an internal ribosome entry site (IRES);

Q is the heterologous gene sequence, including a translation start codon; and

A, B, and C are, separately, optional linker sequence[s];

wherein the DNA construct further comprises a polyadenylation signal at the 3' (downstream) end of Q and a splice acceptor site located 5' (upstream) of ~~Q~~ P.

Claim 23. (Original): A method according to Claim 22 where the heterologous gene coding sequence is randomly inserted into an endogenous gene so that transcription of the heterologous gene coding sequence is directed by the host regulatory elements of the endogenous gene.

Claim 24. (Original): A method according to Claim 22 in which the splice acceptor permits functional integration of the heterologous gene coding sequence into an intron sequence.

Claim 25. (Previously Canceled)

Claim 26. (Original): A method according to Claim 22 further comprising the step of identifying cells expressing the heterologous gene coding sequence.

Claim 27. (Previously Amended): A method according to Claim 26 wherein the construct also comprises a gene encoding a selectable marker and the method comprises selecting cells that express the selectable marker.

Claim 28. (Previously Amended): A mouse embryonic stem cell comprising a heterologous gene code sequence inserted by the method of Claim 22.

Claim 29. (Previously Amended): A descendant of the mouse embryonic stem cell according to Claim 28, wherein the descendant has inherited the inserted heterologous gene coding sequence.

Claims 30-31. (Withdrawn)

Claim 32. (Currently Amended): A DNA construct for randomly inserting a heterologous gene sequence into a mouse cell genome, said heterologous gene sequence lacking a promoter and comprising the sequence:

5' X-A-P-B-Q-C-Y 3'

in which

X and Y	are separately, DNA sequences substantially homologous with a host gene locus;
P	is an internal ribosome entry site (IRES);
Q	is the heterologous gene sequence, including a translation start codon; and
A, B and C	are, separately, optional linker sequence[s];

wherein the DNA construct further comprises a polyadenylation signal at the 3' (downstream) end of Q and a splice acceptor site located 5' (upstream) of ~~Q~~ P.

Claim 33. (Original): A DNA construct according to Claim 32 in which the splice acceptor permits functional integration of the heterologous gene into an intron sequence.

Claim 34. (Previously Amended): A DNA construct according to Claim 32 in which the construct also comprises a gene encoding a selectable marker to facilitate selection of mouse cells containing a heterologous gene that has been inserted into an endogenous gene.

Claims 35-40. (Previously Canceled)

Claim 41. (Previously Amended): A method according to Claim 22 wherein the construct also comprises a gene encoding antibiotic resistance, and the method comprises selecting cells that express the antibiotic resistance.

Claim 42. (Previously Amended): A DNA construct according to Claim 32 wherein the construct additionally comprises a gene encoding antibiotic resistance.

Claims 43-46. (Previously Canceled)

Claims 47-72. (Withdrawn)

Claim 73. (Previously Added): A DNA construct for inserting a heterologous gene coding sequence into a target endogenous gene in a eukaryotic cellular host cell genome, wherein the construct comprises the elements:

5' X-A-P-B-Q-C-Y 3'

in which

X and Y	are substantially homologous with separate sequences from the target endogenous gene and are of sufficient length to undergo homologous recombination with the host cell genome so as to insert the A-P-B-Q-C elements into the host cell genome;
P	is an internal ribosome entry site (IRES);
Q	is the heterologous gene coding sequence; and
A, B, and C	are, separately, linker sequence or a covalent bond.

Claim 74. (Previously Added): The DNA construct according to Claim 73, wherein the construct also comprises a gene encoding a selectable marker.